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AMRL-TDR-62-136

THE VENTILATORY RESPONSE TO CARBON DIOXIDE AND TO OXYGEN AFTER ACCLIMATIZATION TO CARBON DIOXIDE

TECHNICAL DOCUMENTARY REPORT No. AMRL-TDR-62-136

NOVEMBER 1962

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6570th AEROSPACE MEDICAL RESEARCH LABORATORIES
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

Contract Monitor: Donald A. Rosenbaum
Project No. 7163, Task No. 716302

(Prepared under Contract No. AF 33(616)-6261
by
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Chapel Hill, North Carolina)

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Unclassified report

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2. Oxygen
3. Laboratory animals
4. Respiration (physiology)

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FOREWORD

This study was initiated by the Biomedical Laboratory of the 6570th Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio. The research was conducted by the University of North Carolina School of Medicine of Chapel Hill, North Carolina, under Contract No. AF 33(616)-6261. Dr. Thomas B. Barnett and Dr. Richard M. Peters were the principal investigators for the University of North Carolina. Donald A. Rosenbaum, Respiration Section, Physiology Branch, Biomedical Laboratory, served as contract monitor for the 6570th Aerospace Medical Research Laboratories. The work was performed in support of Project No. 7163, "Physiology Research," and Task No. 716302, "Vital Organ Functions in Mammals." The research sponsored by this contract was started in February 1960 and was completed in May 1962.

The experiments reported herein were conducted according to the "Principles of Laboratory Animal Care" established by the National Society for Medical Research.

ABSTRACT

A chamber has been designed so that dogs can be exposed for prolonged periods to abnormal atmospheres. The concentrations of CO_2 and O_2 are continuously controlled and recorded. Exposure of dogs to approximately 3 percent CO_2 in air for 6 days or more resulted in a decrease in the ventilatory response to CO_2. In control dogs the breathing of 50 percent oxygen for 30 minutes was associated with a slight to moderate increase in ventilation without a significant change in arterial pCO_2. After acclimatization to CO_2 oxygen breathing was associated with little change in ventilation but with a rise in arterial pCO_2.

PUBLICATION REVIEW

This technical documentary report has been reviewed and is approved.

Jos M Quashnock

JOS. M. QUASHNOCK
Colonel, USAF, MC
Chief, Biomedical Laboratory

Introduction

Studies have been carried out in the past concerning the effects of artificially increased respiratory dead space in dogs (ref. 1). More recently (ref. 2) it has been shown that when added dead space was maintained for a period of three days, breathing 50 percent oxygen was associated with a significant fall in ventilation and rise in arterial pCO_2. This occurred without any evidence of an altered ventilatory response to CO_2 other than that attributable to increase in the work of breathing. In order to study the effects of various combinations of prolonged hypercapnia, hypoxia and increased work of breathing upon the ventilatory responses to oxygen and to CO_2 a controlled atmosphere chamber has been designed and constructed.

Methods

Chamber Design*

The chamber is designed so that an animal can be exposed to an atmosphere containing abnormal but controlled concentrations of oxygen and CO_2. The temperature of the chamber is also controlled and the air filtered through a plenum containing both a charcoal filter and an absolute filter. The air in the chamber is forced by a centrifugal blower out the top of the chamber, down through a duct, and through a roughing filter prior to entering the other filtering system; it then goes through the cooling coil and then back into the top of the chamber. The flow rate through the circulating system is approximately 30 cubic feet per minute. A sanitary drain connected with a 4 inch drain pipe is so designed that gases do not escape but waste disposal can be carried out. The chamber is illuminated by fluorescent light situated over a transparent panel in the top of the chamber.

The stainless steel chamber itself is 38 inches in diameter and 46 inches high. Access to the interior is provided by a door 43 inches high and 25 inches wide. Within this door is another pair of smaller doors equipped with sleeves which permit access to the experimental animal without loss of atmosphere from the chamber. The chamber is equipped with a 1 inch diameter gas sample tube which permits the use of the chamber as a source of inspired air when animals are being studied outside of the chamber.

The gas analyser-recorder system consists of four major components mounted in a separate cabinet 42 inches by 24 inches by 30 inches H. They are:

1. Hays** Magno-Condu-Therm Oxygen analyser (0-100 percent range)

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* Design and construction supervised by Astra Inc., Raleigh, N. C.

** The Hays Corporation, Michigan City, Indiana.

2. Hays Differential Condu-Therm CO_2 analyser (0-20 percent range)

3. Hays 2-pen Universal Recorder

4. Air Shields[+] "Dia-pump" Model G-3

The gas sample is withdrawn from the air circulating loop after it has been filtered. Approximately 100 cubic feet per hour (cfh) are pumped from the chamber by the Air-Shields pump. Of this, approximately 2 cfh are withdrawn from the stream by the analyser, the remainder being returned to the chamber at the access panel. The chamber gas is analysed after it leaves the cooling coil. By introducing gases and measuring gas concentration at these points the response time of the system is reduced and the mixing of the introduced gas is improved.

The oxygen analyser measures the oxygen concentration by comparing the thermal conductivity of a part of the sample stream in a strong magnetic field with that of a parallel portion not in the field. Since oxygen is paramagnetic, the heat transfer in the magnetic field will be greater than that not in the field, by an amount dependent on the oxygen concentration.

The carbon dioxide analyser is similar except that, instead of a magnetic field, it compares the thermal conductivities of two portions of the gas stream, one of which has passed through a CO_2 absorber (KOH).

Six cam operated sensitive switches mounted on the back of the recorder case and actuated by the recorder pen shaft control the gas concentration in the chamber. Three of these switches are in the carbon dioxide analyser, and three in the oxygen analyser. These switches are so designed that the concentration of both oxygen and CO_2 can be controlled, and are also connected with solenoid valves so that if oxygen concentrations or CO_2 concentrations are of such magnitudes as to endanger the life of the experimental animal, the power to the chamber is cut off, and a safety vent is opened. At the same time supplies of oxygen, nitrogen and CO_2 into the chamber are stopped, allowing the atmosphere within the chamber to return to that of normal air.

According to the original design of the chamber it was anticipated that the animals' carbon dioxide production would maintain the level of CO_2 in the chamber once the desired concentration had been reached by manual feed-in of CO_2. It later developed that this was not possible, so that alterations were made allowing for automatic feed-in of carbon dioxide through solenoid valves activated by the switches in the control mechanism.

During the initial studies in this chamber it was found that condensation of moisture in the gas sampling tubes constituted a serious problem. A small heat exchanger was therefore introduced in the sampling tubes consisting of a copper coil and an electric lamp mounted in an insulated stainless steel box. This simple modification has solved the problem of condensation.

[+] Air Shields, Inc., Hatboro, Pennsylvania.

Figures 1, 2, and 3 show the chamber and figures 4 and 5 the control cabinet.

Figure 1. Exterior View of Chamber Showing Small Access Doors with Sleeves Removed. The blower pulls room air into the chamber which is exhausted through filter box on the left, thus preventing excessively high concentrations of CO_2. The emergency vent is above the center of the door.

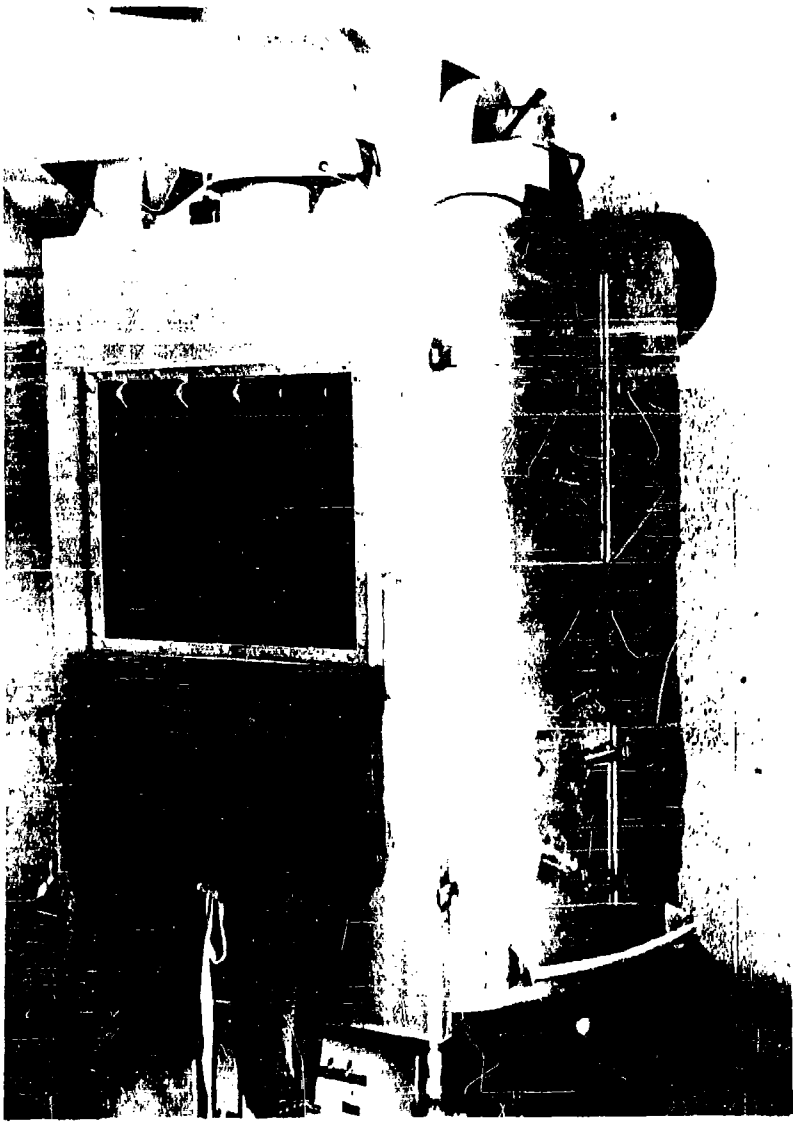

Figure 2. Exterior View of Chamber with Sleeves Attached to Access Door

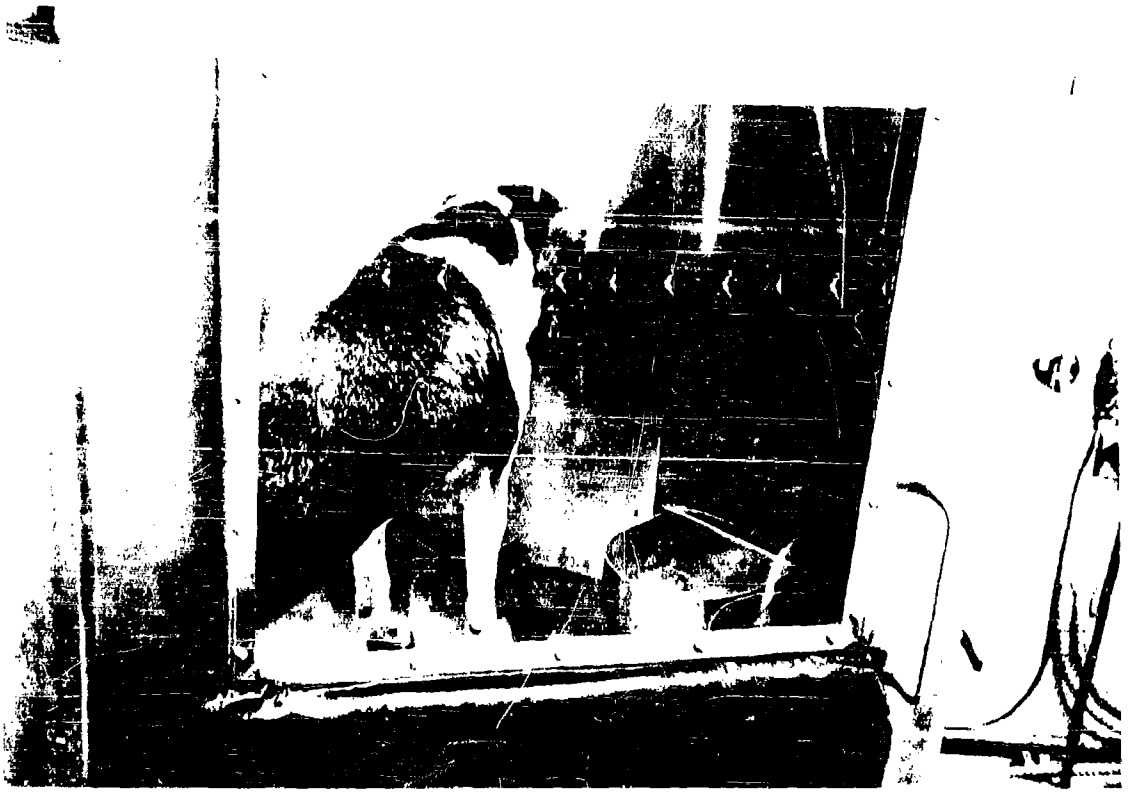

Figure 3. Chamber with Dog Sitting on Shelf Which Is Above Floor of Chamber in Rear

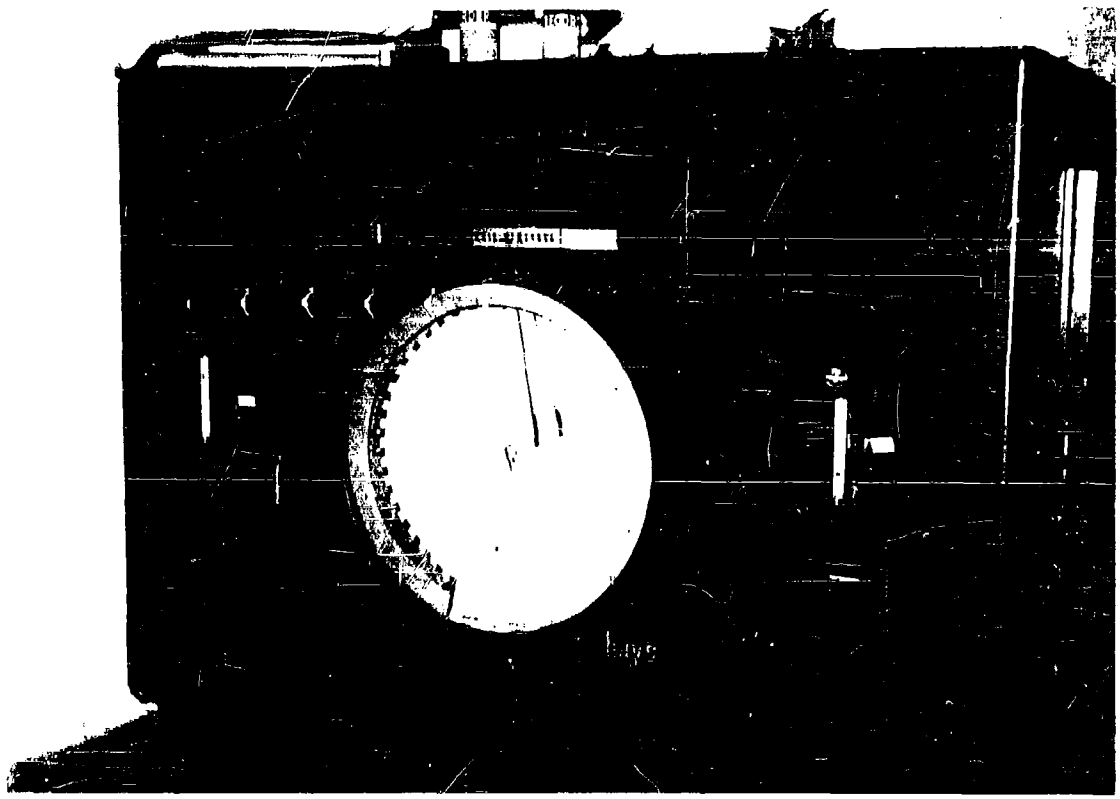

Figure 4. Exterior View of Recorder-Control Cabinet Showing Continuous Record of Gas Concentrations. Flow through the CO_2 analyser cell is regulated by the small flow regulators on either side of the graph.

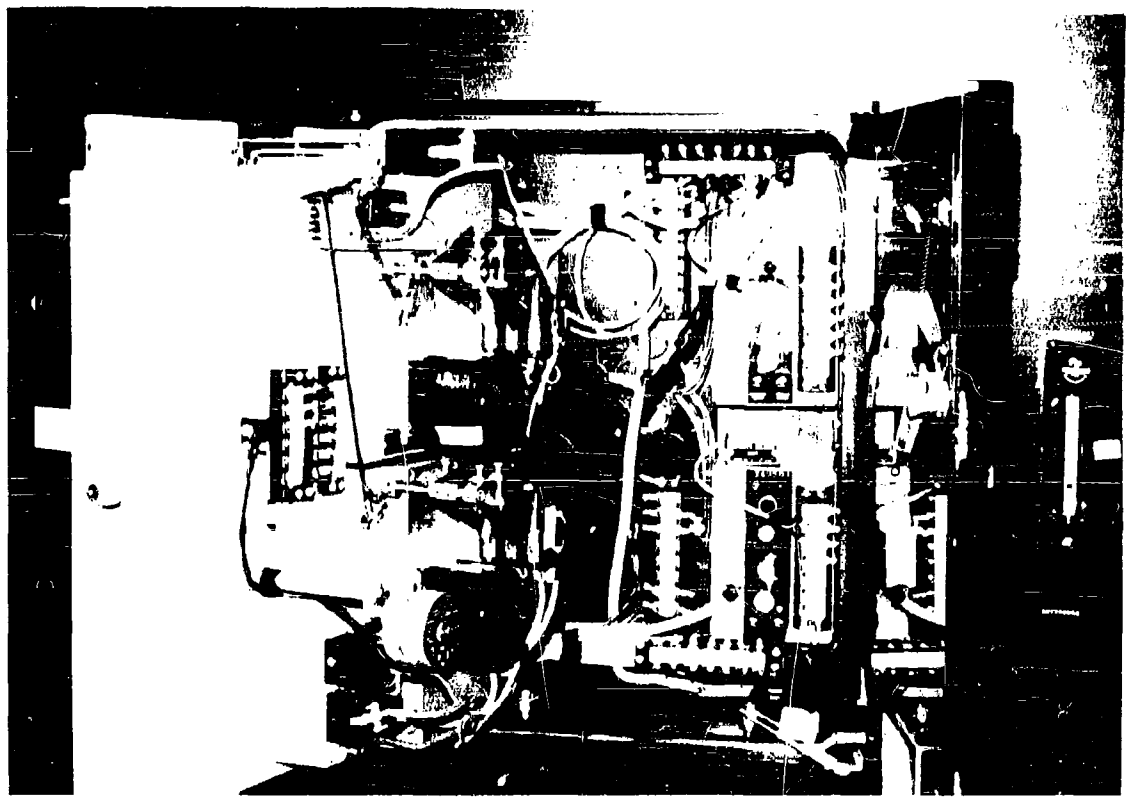

Figure 5. Interior View of Recorder Control Cabinet

Experimental Procedure

Mongrel dogs weighing between 12 and 20 kilograms were studied after a period of training. No anesthesia or sedation was used. Tracheostomies were done using the technique of McIlreath, Craige, and Anzalone (ref. 3), which made possible measurements of ventilation without the use of masks.

During the ventilatory studies the dogs were placed in the lateral position with the upper hind leg suspended in a sling and the lower leg tied firmly to the table. After infiltration with 1 percent lidocaine, an 18-gauge Cournand needle was inserted into the femoral artery. Arterial blood samples were collected anaerobically in heparinized syringes. Duplicate determinations were made of whole blood pH using a Radiometer pH meter and plasma CO_2 content using the Van Slyke-Neill manometric apparatus. Arterial CO_2 tensions were calculated by means of the Henderson-Hasselbalch equation. Arterial oxygen content and capacity were determined by spectrophotometer. A cuffed endotracheal tube was attached through a short Y-tube to a two-way set of plastic J-valves to permit collection of expired air in a Tissot spirometer equipped with a recording kymograph. This arrangement made possible the recording of minute volume and respiratory rate.

Respiratory rate, minute ventilation, arterial pCO_2 and oxygen saturation were measured while the dog breathed room air. These observations were repeated after 30 minutes of breathing 50 percent oxygen in nitrogen. On the following day these measurements were repeated while the dog breathed room air and again after breathing either 5 or 6 percent CO_2 for 10 to 15 minutes.

After all of the above control studies were completed the animal was placed in the controlled atmosphere chamber and allowed to remain there for six days. The oxygen concentration in the chamber was maintained between 21 and 25 percent, the CO_2 concentration between 2.5 and 3.5 percent. At the end of this period the measurements of ventilation, arterial pCO_2 and oxygen saturation were repeated in the following sequence: 1) while the dog breathed chamber air, 2) after 30 minutes of breathing a gas mixture from a Douglas bag containing identical concentration of CO_2 as the chamber air but with 50 percent oxygen (the CO_2 concentrations in the chamber and in the Douglas bag were checked with a Capnograph infra-red carbon dioxide analyser), 3) after returning to chamber air for 30 minutes, and 4) after 10 to 15 minutes of breathing 6 percent CO_2, 25 percent oxygen, 69 percent nitrogen. In this manner, the ventilatory response to CO_2 was measured under circumstances identical to those under which the effects of oxygen breathing were studied. In one animal the CO_2 exposure was carried out at from 1.5 to 2.0 percent CO_2; all other studies were done under the conditions described above.

Results

Figure 6 shows the ventilatory response to inhaled carbon dioxide before and after exposure to approximately 3 percent CO_2. It is apparent that

the slope of this response line is less steep in all instances after acclimatization to carbon dioxide (dotted lines) than it was prior to the period of CO_2 exposure and that the line is shifted to the right after acclimatization. In the one instance where the concentration of CO_2 in the chamber was 1.5 to 2.0 percent (not shown), there was no significant change in slope or position.

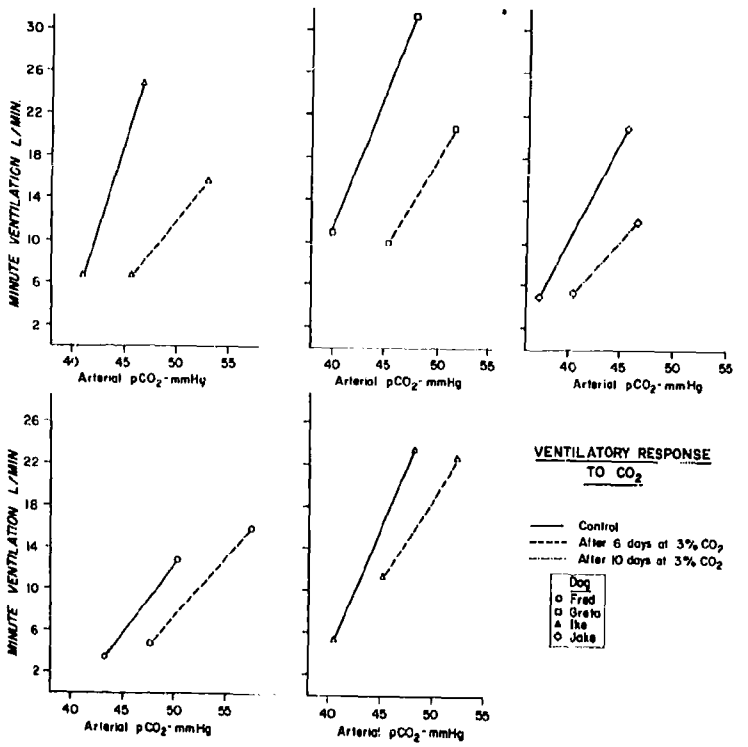

Figure 6. Ventilatory Response to CO_2 Before and After Exposure to 3 Percent CO_2

Figure 7 shows the alveolar ventilation expressed as the ratio of alveolar ventilation on oxygen to that on room air. Measurements were made at 5 minutes, 15 minutes and 30 minutes after starting 50 percent oxygen. Although there were minor variations in ventilation both in the control studies and in studies performed after six days' exposure to 3 percent CO_2, there was no marked difference when the two groups of studies were compared. There was a tendency, however, for ventilation to increase slightly with oxygen in the controls, an observation that has been made in most control dogs in earlier studies.

In one animal (dotted lines in figure 7) the measurement of ventilation on 50 percent oxygen was discontinued when the cuff on the endotracheal tube became deflated. With replacement of another endotracheal tube there resulted, inadvertently, partial obstruction of the airway. Breathing of 50 percent oxygen in this situation resulted in marked depression of respiration.

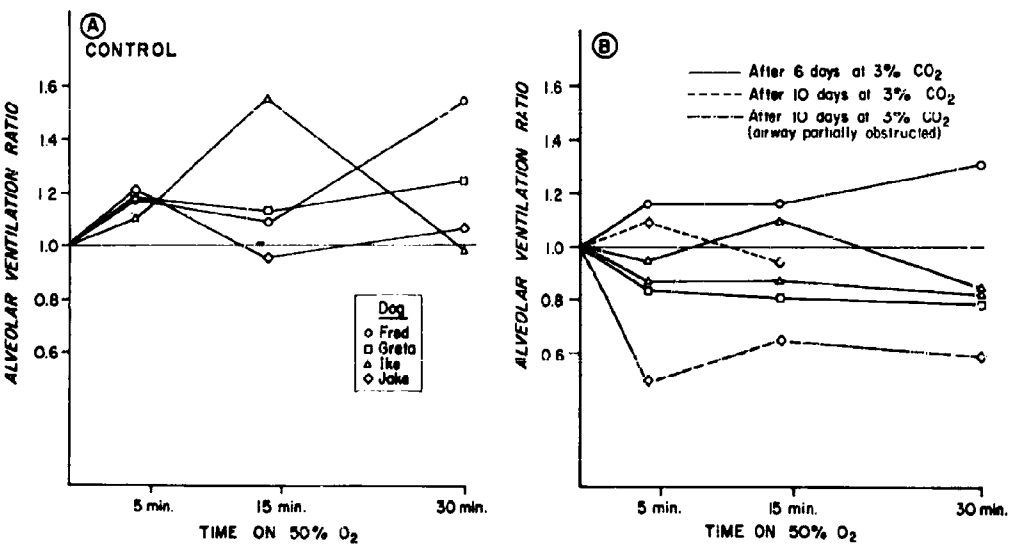

Figure 7. Ventilation While Breathing 50 percent O_2 Before and After Acclimatization to CO_2

Figure 8 shows the effect of oxygen breathing on the arterial pCO_2 before (figure 8A) and after (figure 8B) the six-day exposure to 3 percent CO_2 in the chamber. Whereas in the control studies, as in all previous control studies of this type, breathing 50 percent O_2 had no appreciable effect on arterial pCO_2, after prolonged exposure to CO_2 the breathing of 50 percent oxygen was associated with a slight to moderate rise in pCO_2.

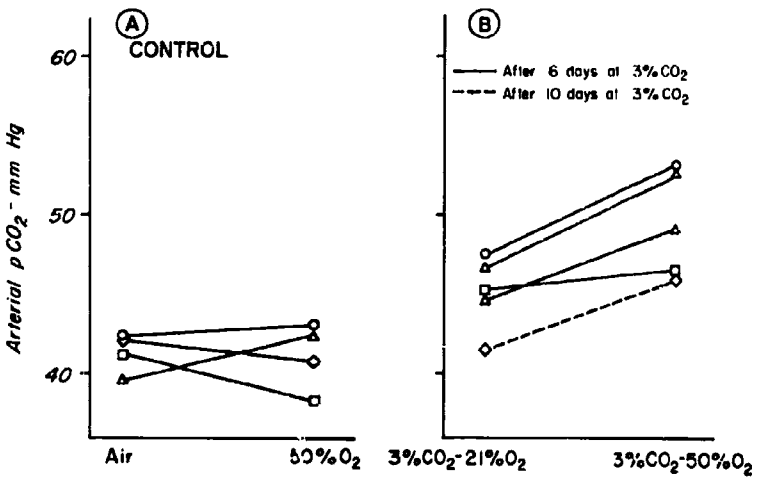

Figure 3

Figure 8. Effects of Oxygen Breathing on Arterial pCO_2 Before and After Acclimatization to CO_2

Discussion

In studies previously reported (ref. 2) it was demonstrated that dogs with increased respiratory dead space for three days exhibited a significant fall in ventilation and rise in arterial pCO_2 when allowed to breathe 50 percent oxygen. These dogs behaved in a sense like patients with chronic alveolar hypoventilation, hypercapnia, hypoxia and increase in the work of breathing. In our studies, it was not possible to demonstrate a change in the ventilatory response to CO_2 during this 3-day period other than that attributable to the increase in respiratory work. It was not possible, however, to determine from these studies whether or not acclimatization to carbon dioxide without hypoxia and without added work of breathing would be associated with oxygen-induced hypoventilation.

The present studies demonstrate that when dogs are maintained in an atmosphere of 3 percent CO_2 for six days they show a diminished response to carbon dioxide as a ventilatory stimulus. Similar results have been reported by Schafer (ref. 4) and by Chapin, Otis, and Rahn (ref. 5) using human subjects. In these dogs that had become acclimatized to carbon dioxide there was little or no decrease in ventilation when they were allowed to breathe 50 percent oxygen, suggesting that a diminsihed ventilatory response to CO_2 in the absence of hypoxia and increased work is not the cause of the abnormal response to oxygen breathing observed in earlier studies. Oxygen breathing was, however, associated with a slight to moderate rise in arterial pCO_2, which must be explained on some basis other than hypoventilation.

A number of investigators have observed a rise in venous pCO_2 with oxygen breathing and Baker and Hitchcock (ref. 6) attributed the observed increase in ventilation in human subjects who breathed 100 percent oxygen to an increase in pCO_2 and hydrogen ion concentration in the respiratory centers of the medulla. It seems possible that a similar tendency toward a rise in pCO_2 may have occurred in our animals. In the control dogs a slight but consistent net increase in ventilation occurred. In the acclimatized dogs the ventilatory response to CO_2 had been lowered, thus explaining their failure to hyperventilate sufficiently to avoid some rise in arterial pCO_2. Certainly this observation in acclimatized animals deserves further study.

The fall in ventilation in one animal with partial airway obstruction while breathing oxygen is of particular interest. Further investigation of acclimatization combined with airway obstruction is in progress.

Summary

A special chamber has been designed for exposing animals to abnormal but controlled atmospheres.

The ventilatory response to carbon dioxide and to 50 percent oxygen has been studied in trained unanesthetized dogs before and after six days' exposure to 3 percent CO_2. Whereas there was a consistent diminution in the ventilatory

response to CO_2 after this period of acclimatization, the breathing of 50 percent oxygen failed to alter ventilation.

Arterial pCO_2 rose slightly to moderately in dogs allowed to breathe 50 percent oxygen after acclimatization to CO_2. The possible mechanism of this finding is discussed.

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